

In the Specification

Applicants present replacement paragraphs below indicating the changes with insertions and deletions indicated by underlining and strikeouts, respectively.

A paper copy of a Substitute Sequence Listing is included herewith. The Substitute Sequence Listing (paper and diskette) has been filed at Mail Stop Sequence. Please replace the pending Sequence Listing with the Substitute Sequence Listing. A copy of the Statement under 37 C.F.R. §1.821(f) and 1.825(a) and (b) is also provided herewith.

Please amend the following paragraphs beginning at page 13, line 1 as follows:

Figure 2: Expression of a mitochondrially targeted Ena/VASP-binding protein sequesters all Mena and VASP, but leaves other focal adhesion proteins in place. Figure 2 depicts a schematic diagram of mito targeting constructs. DFPPPP is SEQ ID NO.: 12. DAPPPP is SEQ ID NO.: 13.

Figure 3: Sequestration of Ena/VASP proteins stimulates cell motility. (a) Cell paths during a 4.5 hour random migration experiment. Dots show centroid positions at 5 minute intervals. (b) Box and whisker plots of cell speeds. Data was analyzed as in figure 1b (ANOVA p-value < 0.0001). FPPPP is SEQ ID NO.: 3. APPPP is SEQ ID NO.: 4.

Figure 4: Depletion of Ena/VASP proteins from focal adhesions, but not the leading edge, has no effect on cell motility. (a) Schematic diagram of cytoplasmic construct. (b) Box and whisker plots of cell speeds (p-value from student's t-test was >0.05). FPPPP is SEQ ID NO.: 3. DFPPPP is SEQ ID NO.: 12.

Figure 5: Constitutive targeting of Ena/VASP proteins to the plasma membrane inhibits cell motility. (a) Schematic diagram of membrane targeting constructs (b) Immunofluorescence analysis of FPPPP-CAAX (SEQ ID No.: 7) and APPPP-CAAX (SEQ ID NO.: 8) expressing cells. (c) Box and whisker plots of cell speed (ANOVA p-value < 0.0001).

Figure 6: Protrusion and retraction, independent of cell translocation, positively correlates with speed. (a) Diagram illustrating positive and negative membrane flow. The outlines of the same cell in two adjacent frames are overlaid, new areas of protrusion are indicated in green, areas of retraction are in red. (b) Box and whisker plot of average flow per 10

minute time period. Average flow calculated by averaging the absolute values of positive and negative flow and is expressed as a % of total cell area from the first frame (ANOVA p-value < 0.0001). FPPPP is SEQ ID NO.: 3. FPPPP-CAAX is SEQ ID NO.: 7.

Figure 7: Complementation of Ena/VASP-deficient cells slows motility. Box and whisker plots of cell speed of MV^{D7} and MV^{D7}/EGFP-Mena cells (ANOVA p-value < 0.0001). FPPPPP is SEQ ID NO.: 3.

Figure 8: Known properties of Ena/VASP Proteins. Schematic diagram illustrating conserved domains within the Ena/VASP protein family. D/EFPPPP is SEQ ID NO.: 1.

Please amend the following paragraph beginning at page 14, line 18, as follows:

SEQ. ID. NO. 1 is the protein consensus motif D/E FPPPPX D/E D/E FPPPPXDDE.

Please insert the following paragraphs beginning at page 14, line 28, as follows:

SEQ. ID. NO. 12 is the protein consensus motif DFPPPP.

SEQ. ID. NO. 13 is the protein consensus motif DAPPPP.

SEQ. ID. NO. 14 is the protein consensus motif D/EFPPPP.

Please amend Table 1, beginning on page 63, at line 17, as follows:

Table 1

Number of Focal Adhesions per Cell (± SD)	Rat2			
	EGFP-Mena (high)		DFPPPP-mito <u>SEQ ID NO.: 12</u>	DAPPPP-mito <u>SEQ ID NO.: 13</u>
Vinculin ⁺	86.6 ± 16.0	72.7 ± 14.4	79.5 ± 17.7	81.6 ± 13.9
Zyxin ⁺	79.6 ± 26	73.6 ± 20	75.8 ± 19	79.2 ± 29

Please amend following paragraph beginning at page 73, line 23 as follows:

Results

Figure 8 is a schematic diagram depicting the known properties of Ena/VASP proteins. The properties conserved among the known Ena/VASP proteins include an EVH1 domain which is known to bind to D/EFPPPP (SEQ ID No.: 14). The EVH1 domain is believed to

play a role in focal adhesion targeting. Another conserved domain known as the proline rich domain is also shown in Figure 8. The proline rich domain binds to profilin and SH3, WW. This domain is believed to play a role in actin dynamics. A third conserved domain is referred to as EVH2. The EVH2 domain binds to actin and is involved in the mediation of actin dynamics and oligomerization. In addition to the conserved domains, two phosphorylation sites are highly conserved within Ena/VASP proteins. These phosphorylation sites are designated in Figure 8 with a *.